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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,887	12/11/2001	Geoffrey W. Krissansen	8654/2072	2382

29933 7590 12/07/2005

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EXAMINER	
YAO, LEI	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 12/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/014,887	KRISSANSEN ET AL.	
	Examiner	Art Unit	
	Lei Yao, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-47* is/are pending in the application.

4a) Of the above claim(s) *10-11,15,18-19, 23, 26-27, 31, 34-35, 39, 42-43, 47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-9, 12-14, 16-17. 20-22, 24-25, 28-30, 32-33, 36-38, 40-41, 44-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/16/03, 1/27/03/*. 519-02
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed on 10/6//05 in response to the previous Non-Final Office Action (4/5/05) is acknowledged and has been entered.

Claims 5 and 48-55 have been cancelled. Claims 10-11, 15, 18-19, 23, 26-27, 31, 34- 35, 39, 42-43, 47 have been withdrawn for non-elected invention. Claims 1-4, 6, 12-13, 20-21, 28-29, 37, 40, 44-46 have been amended. **Claims 6-7** will be joined for examination in view of the amendment of the claims. Claims 1-4, 6-47 are pending. Claims 1-4, 6-9, 12-14, 16-17, 20-22, 24-25, 28-30, 32-33, 36-38, 40-41, 44-46 are under consideration.

The following office action contains NEW GROUNDS of rejection.

Information Disclosure Statement

The information disclosure statement (s) (IDS) submitted on 1/28/03, 5/9/02, and 5/16/2003 are/is considered by the examiner and initialed copy of the PTO-1449 is enclosed.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in New Zealand on 6/14/1999. It is noted, however, that applicant has not filed a certified copy of the NZ336259 application as required by 35 U.S.C. 119(b).

Rejections Withdrawn

The rejection of claims 1-4, 8-9, 12-14, 16, 17, 20-22, 24, 25, 28-30, 32-33, 36-38, 40, 41, and 44-46 under 35 U.S.C. 102(b) as being anticipated by Pedley et al (Cancer Research, Vol, 56, p3293-3300, 1996) is withdrawn in view of the amendments to the claims.

Response to Arguments

Election of Restriction

Withdrawal of claims 15, 23, 31, 39, and 47 for examination is maintained for the reasons of record in the prior Office Action (4/5/05).

This has been carefully considered but is deemed not to be persuasive. The response states that that the claims 15, 23, 31, 39, and 47 were erroneously withdrawn form consideration since the claims are directed to the subject matter of the Group I and encompassed by the tumor growth restricted agent election, analogs of XAA. In response to this argument, The Applicant elect species, analogs of XAA as a tumor growth-restricting agent, however, the claims 15, 23, 31, 39, and 47 are directed to hypoxia-inducible factor (HIF) as a tumor restricted agent, which is a structurally and functionally different molecule from XAA. Search HIF and XAA together would impose serious search burden. Therefore, 15, 23, 31, 39, and 47 are withdrawn from further consideration at this time by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species.

The following is a New Ground of rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6-9 and 12-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factor considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re wands,* 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir.1988).

The set of claims is **broadly drawn** to a method of treatment for a mammal, with advanced or large tumor burdens, comprising the administration to said mammal of **a protein** of T-cell co-stimulatory cell adhesion molecule (CAM) in conjunction with a tumor growth-restriction agent comprising DMXAA, either of which alone would **be ineffective** in retarding or eradicating an advanced or large tumor burden.

To satisfy the requirement of 112, 1st paragraph, it is necessary that the specification provide an enabling disclosure of how to make and use a claimed invention. The method objective of claims is a method for using two reagents together comprising using CAM protein treating advanced or large tumor **because one of the reagents is ineffective**. Thus, it would be expected that state of the prior art has **already known** that **CAM in any form comprising gene deliver B7.1 or administering the protein of B7.1 or DMXAA alone is ineffective** in treating advanced or large tumor.

The specification, on para 83, paragraph 7, states that B7.1 mediated anti-tumor immunity is accompanied by argument of **CTL and apoptosis** of tumor cells. The specification teaches a method of gene transfer of B7.1 by liposome system for treating a tumor (para 66). The specification also states there is a predominance of necrotic cells in tumor section from DMXAA-treated mice (para 83). The specification **seems teach away** that either B7.1 or DMXAA alone is ineffective in treating advanced or large tumor. The specification does not teach administering **B7.1 protein alone** or in combination with DMXAA in treating a tumor. The specification does not provide any teaching on treating for a mammal with a tumor by administration to a mammal of CAM protein comprising **B7.1 protein** in conduction with DMXAA. Thus, the instant specification fails to disclose the necessary parameters for using the method, which would lead to treating for a mammal with a tumor by administration to a mammal of CAM protein comprising B7.1 protein in conjunction with DMXAA, and either of the two agents alone is ineffective in treating tumor.

Since the specification does not provide claimed method for treating a tumor with B7.1 protein with DMXAA for retarding or eradication an advance or large tumor burden and since the specification does not provide enough evidence for each reagent having no effect when they are using alone for cancer treatment. One skilled in the art would not expect the claimed method will be successful in use the claimed method for treating cancer on the basis of teachings in the prior art or instant specification.

In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to treating a cancer with CAM protein and DMXAA, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquires set forth in Graham V. john Deere Co., 383 U.S. 1, 148 USPQ 459 (1996), that are applied for establishing a background for determining obviousness under 25 U.S. C. 103 (a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or obviousness

Claims 2-4, 16-17, 20-22, 24-25, 28-30, 32-33, 36-38, 40-41, 45-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Futami et al., (J of Immunotherapy, vol 12, 247-255) in view of Olsson et al., (International Immunology, vol 10, page 499-506).

The sets of claims are drawn to methods of treating a patient with cancer or potentiating the activity of tumor restricted agent comprising an analogue of Xanthenone-4 acetic acid (XAA) or 5, 6 dimethylxanthenone-4-acetic acid (DMXAA) for treating cancer by administering T-cell co-stimulatory cell adhesion molecule (CAM) comprising B7.1, CD80 antigen, in conjunction with analogue of XAA.

Futami et al., teach a method of treating tumor by analogues of XAA in conjunction with a T-cell stimulating molecule, IL-2. Futami et al., teach that the activity of analogues of XAA can be potentiated by recombinant IL-2 in treating a tumor. Futami et al., also teach a method of treating cancer by administering a subject both reagents (page 249, column 1-2 and page 251, column 1).

Futami et al., do not teach that treating cancer with analogue of XAA in conjunction with CAM.

Olsson et al., teach Human IL-2 is induced by CD80 (B7.1, a CAM molecule) in cancer cells and T cells (entire article).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to use the method to eradicate any advanced or large tumor by administering analogues of XAA in combination of CAM comprising CD80 with the expected result for cancer treatment. It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to potentate the activity of single reagent for cancer treatment by a second reagent. One of ordinary skill in the art would have been motivated with a reasonable expectation of success to combine the teachings of Olsson et al., to the teaching of Futami et al., to treat cancer by combining CAM and analogues of XAA comprising DXMAA because Futami et al., have shown that IL-2 and analogues of XAA have a synergy effect when they are used for cancer therapy and Olsson et al., have shown IL-2 can be induced by a CAM, CD80. One of ordinary skill in the art would have been motivated with a reasonable expectation of success use CAM and analogues of XAA together, or administering one reagent prior to another, or administering additional analogues of XAA for cancer treatment.

Conclusion

NO claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-4.30pm Monday to Friday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao, Ph.D.
Examiner
Art Unit 1642

LY

SHEELA HUFF
PRIMARY EXAMINER